REMARKS

This is in response to the Office Action mailed on March 1, 2006. Claims 1-35 are pending in the application. In the Office Action, claims 1-35 were rejected. No amendments have been made to the claims.

The Office Action rejected claims 1-35 under 35 U.S.C. §103(a) as being unpatentable over Carlyle et al. International Publication No. WO 99/37337 (the Carlyle application) in view of U.S. Patent No. 6,124,131 (the Semenza patent) or Tsuzuki et al. (the Cancer Research Article). The Office Action alleges that the Carlyle application teaches a medical device on which VEGF has been attached to promote population of the device with viable cells and other positive results. The Office Action further alleges that the Carlyle application teaches all the claimed devices in detail through the reference and also details means for attaching the peptide to the device in all of the methods Applicants claim. The Office Action further alleges that the Carlyle application teaches all of the claimed limitations except that the reference uses VEGF and does not teach using a VEGF stimulation compound. The Office Action then alleges that at the time that the invention was made, it would have been obvious to one of ordinary skill in the art to substitute a known VEGF stimulation compound for the VEGF used by the Carlyle application because such a compound would have caused the production of a desired compound VEGF.

The Office Action admits that the Carlyle application does not teach using HIF-1α as the stimulator/agonist of VEGF. However, the Office Action alleges that it would have been obvious at the time the invention was made to use HIF-1α in lieu of VEGF in the process disclosed in the Carlyle application or device disclosed in the Carlyle application because the Semenza patent and Cancer Research Article teach that HIF-1α is a known

stimulator of VEGF.

Applicants respectfully disagree that claim 1 is made obvious by the Carlyle application in view of either the Semenza patent or the Cancer Research Article. Elements of claim 1 include a medical device comprising a stimulation compound associated with the medical device wherein the stimulation compounds stimulates production of VEGF, the medical device being an implantable medical device, a catheter, a dressing or a surgical instrument.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). There is no disclosure in any of the cited references of a medical device having a stimulation compound associated therewith where the stimulation compounds stimulates production of VEGF.

The Carlyle application teaches the use of VEGF and VEGF-related compounds in association with prostheses to stimulate chemotaxis and cell growth (see p. 8, l. 1-14 of the Carlyle application, for example). The Carlyle application does not disclose or teach use of a stimulation compound associated with a medical device to stimulate production of growth factors. Further, the Carlyle application does not disclose a stimulation compound, such as HIF-1α, to stimulate production of VEGF.

Next, the Office Action alleges that the Semenza patent and the Cancer Research Article teach that HIF-1α can be substituted for the VEGF disclosed in the Carlyle application to stimulate production of VEGF. Neither the Semenza patent nor the Cancer Research Article, either singly or in combination with the Carlyle application, teach or suggest associating a stimulation compound, such as HIF-1α, with a medical device that stimulates production of VEGF as claimed in claim 1. Further, neither the Semenza patent nor the Cancer Research Article teach using HIF-1α as a stimulation compound for the production of VEGF to be

associated with a medical device. Therefore, there is no teaching or suggestion in either the Carlyle application, the Semenza patent or the Cancer Research Article to combine the references to allege that claim 1 is obvious.

There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). The Carlyle application addressed issues relating to the biocompatibility of an implanted prosthesis. The Semenza patent addresses the discovery of HIF-1α as a VEGF promoter. The Cancer Research Article addresses the effect of HIF-1α on the production of VEGF and the effect of VEGF on the growth rate of tumors.

The problems to be solved or the discovery disclosed in each of the references are unrelated. Absent the present invention in claim 1, there is no motivation to combine the Carlyle application with either the Semenza patent or the Cancer Research Article. Therefore, the combination of the Carlyle application with the Semenza patent or the Cancer Research Article is improper, and claim 1 is not obvious.

Further, Applicants disagree with the Office Action that: "The coating of a VEGF stimulating compound on a medical device would produce the same desired results sought by Carlyle." Applicants acknowledged the Carlyle application at page 25, lines 18-22. However, Applicants believed that the claimed medical device in claim 1 was sufficiently different from the disclosure of the Carlyle patent and provided advantages over the Carlyle patent such that the claimed invention was not obvious over the Carlyle patent.

The specification discloses several reasons for or advantages of utilizing a stimulation compound to produce VEGF in comparison to coating a medical device with VEGF. For instance,

the reasons or advantages include, but are not limited to:

> The HIF and/or other stimulation compounds direct natural processes that encourage cellular activity and vascularization near the medical device without the effort associated with in vitro manipulation of cells.

Page 5, lines 19-21.

> Incorporation of a stimulation molecule capable of stimulating VEGF production near the surface of a medical device, such as a heart valve prosthesis, or a portion thereof, could reduce the risk of thrombosis and the long-term need for anticoagulation therapy.

Page 6, lines 2-5.

> The stimulation compound generally is releasably associated with the biocompatible material such that the stimulation compound is gradually released into the fluids and/or tissue surrounding the medical device.

Page 18, lines 8-10.

> While the stimulation compound stimulates the generation of VEGF in the vicinity of the biocompatible material, it may be desirable to also have VEGF associated with the biocompatible material. ... Thus, the combined use of an associated stimulation compound and associated VEGF can have a synergistic effect with respect to promoting the colonization of the biocompatible material.

Page 25, lines 5-7, 13-15.

> In other embodiments, a portion of biocompatible material with associated stimulation compounds is placed in a cell culture system as a time release agent to gradually release stimulation compound into the cell culture. Stimulation compound could be desirable in the cell culture system to provide a constant regeneration of VEGF through cellular activity.

Page 28, line 30 - page 29, line 2.

Therefore, associating a stimulation compound with a medical device to produce VEGF clearly does not produce the same results as coating a medical device with VEGF.

For the foregoing reasons, claim 1 is believed to be in allowable form. Reconsideration and allowance of claim 1 are respectfully requested.

Claims 2-30 depend from independent claim 1 and were rejected for the reasons stated with respect to claim 1. While Applicants do not acquiesce to the rejection, the rejection has been overcome for the reasons stated with respect to the allowability of claim 1. Reconsideration and allowance of claims 2-30 are respectfully requested.

The Office Action also rejected independent claim 31 as being obvious for the reasons stated with respect to claim 1. For the reasons stated with respect to claim 1, claim 31 is not obvious and also is in allowable form. Reconsideration and allowance of claim 31 are respectfully requested.

Claims 32-35 depend from independent claim 31 and were rejected for the reasons stated with respect to claim 31. While Applicants do not acquiesce to the rejection, the rejection has been overcome for the reasons stated with respect to the allowability of claim 31. Reconsideration and allowance of claims 32-35 are respectfully requested.

For the foregoing reasons, Applicants believe the present application is in condition for allowance. Reconsideration and allowance of the present application are respectfully requested.

The Director is authorized to charge any fee deficiency

required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

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